

92 (new). A method of screening for the presence of a benign dysproliferative disorder characterized by an aberrant level of a Notch protein or Notch derivative in a patient, comprising measuring the level of expression of a Notch protein or of a Notch derivative capable of being bound by an anti-Notch antibody in a sample derived from the patient, in which an increase or decrease in the Notch protein or derivative in the patient sample relative to the level found in such a sample from individual not having the disorder indicates the presence of the disorder in the patient.

REMARKS

Claims 68-74 have been amended, and new claims 90-92 added, to more particularly point out and distinctly claim that which Applicants regard as the invention. The subject matter of the amended and new claim recitations is fully supported in the specification. In particular, support for the amended recitation "screening for the presence of a malignancy" in claims 68 and 69 is found in the specification at page 5, lines 18-21, and page 37, lines 16-22. While a patent applicant does not have to describe exactly the subject matter claimed, the description must clearly allow persons of ordinary skill in the art to recognize that the applicant invented what is claimed. Vas-Cath, Inc. v. Mahurkar, 935 F.2d 1555, 1563, 19 U.S.P.Q.2d 111, 1116 (Fed. Cir. 1991) (citing In re Gosteli, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989)). The amended recitation "of a Notch protein or of a Notch derivative . . . antibody" of claim 68 is supported in the specification at page 36, lines 15-28. New claim 90 is supported in the specification at page 37, lines 9-15. New claims 91 and 92 are supported in the specification at page 5, lines 18-21; page 20, line 24 to page 23, line 26; and page 36, line 15 to page 37 line 30.

1. The Restriction Requirement

Applicants' election with traverse of Group IX, claims 68-74 is acknowledged by the Examiner. The restriction requirement has been made final, and claims 1-67 and 75-89 have been withdrawn from further consideration by the Examiner as drawn to a nonelected invention. Applicants have thus canceled claims 1-67 and 75-89 without prejudice. Applicants reserve the right to prosecute the subject matters of the nonelected claims in one or more related applications.

2. The Examiner's Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 68-74 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner states that the disclosure is enabling only for claims limited to methods of screening for the presence of malignancies and "nervous system disorders" by measuring the expression of Notch protein¹ and comparing the level of expression with normal levels. The Examiner contends that:

The specification indicates that aberrant (increased or decreased) expression or activity of Notch protein is associated with several dozen conditions. In light of this, confirmation of aberrant expression or aberrant activity of Notch protein alone cannot be used to definitively diagnose or distinguish any particular condition. Similarly, there is no indication that aberrant Notch protein expression or activity is found in virtually all of these particular disorders. Because of this, the instant method is considered to be a method of screening for disorders, rather than a method of diagnosis. Moreover, the specification is enabling only for

¹ The Examiner states parenthetically that "actually, in a patient, this [Notch protein] should be referred to as *TAN-1*, the designation for the human homolog." *TAN-1* has been used by Ellisen et al. (1991, Cell 66: 649-661) to refer to only one of the Notch human homologs. Thus, Applicants respectfully decline to limit the claims to detecting expression only of the TAN-1 Notch protein. Additionally, Applicants are entitled to be their own lexicographer. See Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861 (Fed. Cir. 1985).

claims limited to methods of screening for malignancies or "nervous system disorders." While the specification mentions many examples of each of these broad categories of disorders, no guidance is provided for other conditions which may be associated with aberrant expression or activity of Notch protein. In the absence of further guidance, it would require an undue amount of experimentation for one of ordinary skill in the art to determine whether a condition other than a malignancy or a "nervous system disorder" was present in an individual exhibiting aberrant expression of Notch protein. Finally, the specification is enabling only for measuring aberrant Notch protein expression, as opposed to aberrant activity in a patient. The specification does not define Notch protein "activity," nor does it indicate that the exact function or mechanism of action of the *TAN-1* protein is known. In the absence of any guidance for measuring some parameter of activity or function, it would require an undue amount of experimentation for one of ordinary skill in the art to determine whether or not aberrant Notch protein activity was present in a sample. See MPEP 706.03(n) and 706.03(z)

In response, Applicants have amended the claims such that all the pending claims are limited to screening for the presence of a malignancy (claims 68-74 and 75) or a disease or disorder of the nervous system (claim 76) or a benign dysproliferative disorder (claim 77) by measuring level of expression of a Notch protein or Notch derivative. Applicants note that the specification provides ample guidance to enable screening for benign dysproliferative disorders. See the specification at page 5, line 18-21; in particular, page 23, lines 16-26; and page 36, line 15 to page 37, line 30.

Applicants believe that the amendments to the claims obviate the Examiner's rejection.

CONCLUSION

Applicants respectfully request that the amendments of the present response be entered and made of record in the instant application. An early allowance is earnestly requested. If any issues remain in connection herewith, the Examiner is respectfully invited to telephone the undersigned to discuss the same.

Respectfully submitted,

PENNIE & EDMONDS
Attorneys for Applicants

Date: June 9, 1995
Telephone: (212) 790-9090

S. Leslie Misrock 18,872
S. Leslie Misrock (Reg. No.)

By: Adriane M. Antler 32,605
Adriane M. Antler (Reg. No.)